SEQUENCE LISTING

<110> BAKER, Matthew
WATKINS, John

<120> MODIFIED HIRUDIN PROTEINS AND T-CELL EPITOPES IN HIRUDIN

<130> MER-142

<140> Unknown
<141>

<150> PCT/EP2004/006943
<151> 2004-06-25

<150> EP03014332.5
<151> 2003-06-26

<160> 108

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X=A, G, H, K, N, P,Q, R, V;
X=A,D,E,G,H,K,N,Q,R,S,T,I;

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X=A, T, P

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20 25 30
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Glu Ser His Asn Xaa Gly Asp Xaa Glu Glu Ile Pro Glu Glu Tyr Leu
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20 25 30
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Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
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Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
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Gln
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            20   25   30
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        35   40   45
Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
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            20   25   30
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        35   40   45
Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
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Gln
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            20                  25                  30
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Glu Ser His Asn Glu Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
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            20                  25                  30
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Glu Ser His Asn Asn Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
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Asp Gly Glu Lys Asn Gln Cys Ala Thr Gly Glu Gly Thr Pro Lys Pro
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Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
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            20                  25                  30
Asp Gly Glu Lys Asn Gln Cys Thr Thr Gly Glu Gly Thr Pro Lys Pro
        35                  40                  45
Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
    50                  55                  60
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Glu Gly Ser Val Val Cys Gly Gln Gly Asn Lys Cys Arg Lys Gly Ser
            20                  25                  30
Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
        35                  40                  45
Glu Ser His Asn Glu Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
    50                  55                  60
Gln
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<400> 13
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 1   5   10   15
Glu Gly Ser Val Val Cys Gly Gln Gly Asn Lys Cys Arg Lys Gly Ser
            20   25   30
Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
        35   40   45
Glu Ser His Asn Asn Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
    50   55   60
Gln
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 1   5   10   15
Glu Gly Ser Val Val Cys Gly Gln Gly Asn Lys Cys Arg Arg Gly Ser
            20   25   30
Asp Gly Glu Lys Asn Gln Cys Thr Thr Gly Glu Gly Thr Pro Lys Pro
        35   40   45
Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
    50   55   60
Gln
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 1   5   10   15
Glu Gly Ser Val Val Cys Gly Gln Gly Asn Lys Cys Ala Lys Gly Ser
            20   25   30
Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
        35   40   45
Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
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Gln
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Glu Gly Ser Val Val Cys Gly Gln Gly Asn Lys Cys Ala Gln Gly Ser
            20   25   30
Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
        35   40   45
Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
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Gln
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Glu Gly Ser Val Val Cys Gly Gln Gly Asn Lys Cys Ala Arg Gly Ser
            20   25   30
Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
        35   40   45
Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
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Gln
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Glu Gly Ser Val Val Cys Gly Gln Gly Asn Lys Cys Ala Thr Gly Ser
            20   25   30
Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
        35   40   45
Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
    50   55   60

Gln
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 1   5   10   15
Glu Gly Ser Val Val Cys Gly Gln Gly Asn Lys Cys Asp Ala Gly Ser
            20   25   30
Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
        35   40   45
Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
    50   55   60
Gln
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 1   5   10   15
Glu Gly Ser Val Val Cys Gly Gln Gly Asn Lys Cys Asp Gln Gly Ser
            20   25   30
Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
        35   40   45
Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
    50   55   60
Gln
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<400> 21
Val Val Tyr Thr Asp Cys Thr Glu Ser Gly Gln Asn Leu Cys Leu Cys
 1   5   10   15
Glu Gly Ser Val Val Cys Gly Gln Gly Asn Lys Cys Asp Arg Gly Ser

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            20                  25                  30
Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
        35                  40                  45
Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
    50                  55                  60
Gln
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Glu Gly Ser Val Val Cys Gly Gln Gly Asn Lys Cys Glu Lys Gly Ser
            20                  25                  30
Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
        35                  40                  45
Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
    50                  55                  60
Gln
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 1               5                  10                  15
Glu Gly Ser Val Val Cys Gly Gln Gly Asn Lys Cys Glu Gln Gly Ser
            20                  25                  30
Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
        35                  40                  45
Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
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Gln
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 1   5   10   15
Glu Gly Ser Val Val Cys Gly Gln Gly Asn Lys Cys Glu Arg Gly Ser
            20   25   30
Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
        35   40   45
Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
    50   55   60
Gln
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Glu Gly Ser Val Val Cys Gly Gln Gly Asn Lys Cys Glu Thr Gly Ser
            20   25   30
Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
        35   40   45
Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
    50   55   60
Gln
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 1   5   10   15
Glu Gly Ser Val Val Cys Gly Gln Gly Asn Lys Cys Arg Lys Gly Ser
            20   25   30
Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
        35   40   45
Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
    50   55   60
Gln
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Val Val Tyr Thr Asp Cys Thr Glu Ser Gly Gln Asn Leu Cys Leu Cys
 1   5   10   15
Glu Gly Ser Val Val Cys Gly Gln Gly Asn Lys Cys Arg Gln Gly Ser
            20   25   30
Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
        35   40   45
Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
    50   55   60
Gln
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<400> 28
Val Val Tyr Thr Asp Cys Thr Glu Ser Gly Gln Asn Leu Cys Leu Cys
 1   5   10   15
Glu Gly Ser Val Val Cys Gly Gln Gly Asn Lys Cys Arg Arg Gly Ser
            20   25   30
Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
        35   40   45
Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
    50   55   60
Gln
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Glu Gly Ser Val Val Cys Gly Gln Gly Asn Lys Cys Arg Thr Gly Ser
            20   25   30
Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
        35   40   45
Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
    50   55   60
Gln
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Glu Gly Ser Val Val Cys Gly Gln Gly Asn Lys Cys Ser Ala Gly Ser
            20   25   30
Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
        35   40   45
Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
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            20   25   30
Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
        35   40   45
Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
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Gln
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Glu Gly Ser Val Val Cys Gly Gln Gly Asn Lys Cys Ser Gln Gly Ser
            20   25   30
Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
        35   40   45

Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
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Gln
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Val Val Tyr Thr Asp Cys Thr Glu Ser Gly Gln Asn Leu Cys Leu Cys
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20 25 30
Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
35 40 45
Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
50 55 60
Gln
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<400> 34
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1 5 10 15
Glu Gly Ser Val Val Cys Gly Gln Gly Asn Lys Cys Ser Thr Gly Ser
20 25 30
Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
35 40 45
Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
50 55 60
Gln
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 1               5                  10                  15
Glu Gly Ser Val Val Cys Gly Gln Gly Asn Lys Cys Thr Ala Gly Ser
            20                  25                  30
Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
        35                  40                  45
Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
    50                  55                  60
Gln
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Glu Gly Ser Val Val Cys Gly Gln Gly Asn Lys Cys Thr Lys Gly Ser
            20                  25                  30
Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
        35                  40                  45
Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
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Gln
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Glu Gly Ser Val Val Cys Gly Gln Gly Asn Lys Cys Thr Gln Gly Ser
            20                  25                  30
Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
        35                  40                  45
Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
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Gln
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Glu Gly Ser Val Val Cys Gly Gln Gly Asn Lys Cys Thr Arg Gly Ser
            20   25   30
Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
        35   40   45
Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
    50   55   60
Gln
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<400> 39
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 1   5   10   15
Glu Gly Ser Val Val Cys Gly Gln Gly Asn Lys Cys Thr Thr Gly Ser
            20   25   30
Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
        35   40   45
Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
    50   55   60
Gln
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 1   5   10   15
Glu Gly Ser Val Val Cys Gly Gln Gly Asn Lys Cys Ile Leu Gly Ser
            20   25   30
Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
        35   40   45
Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
    50   55   60
Gln
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<400> 41
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 1   5   10   15
Glu Gly Ser Val Val Cys Gly Gln Gly Asn Lys Cys Ile Leu Gly Ser
            20   25   30
Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
        35   40   45
Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
    50   55   60
Gln
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Val Val Tyr Thr Asp Cys Thr Glu Ser Gly Gln Asn Leu Cys His Cys
 1   5   10   15
Glu Gly Ser Val Val Cys Gly Gln Gly Asn Lys Cys Ile Leu Gly Ser
            20   25   30
Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
        35   40   45
Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
    50   55   60
Gln
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            20   25   30
Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
        35   40   45
Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu

50 55 60
Gln
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Val Val Tyr Thr Asp Cys Thr Glu Ser Gly Gln Asn Leu Cys Thr Cys
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35 40 45
Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
50 55 60
Gln
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20 25 30
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35 40 45
Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
50 55 60
Gln
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1 5 10 15

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Glu Gly Ser Val Gly Cys Gly Gln Gly Asn Lys Cys Ile Leu Gly Ser
            20                  25                  30
Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
        35                  40                  45
Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
    50                  55                  60
Gln
65
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<223> modified hirudin

<400> 47

```
Val Val Tyr Thr Asp Cys Thr Glu Ser Gly Gln Asn Leu Cys Leu Cys
 1               5                  10                  15
Glu Gly Ser Val His Cys Gly Gln Gly Asn Lys Cys Ile Leu Gly Ser
            20                  25                  30
Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
        35                  40                  45
Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
    50                  55                  60
Gln
65
```

<210> 48
<211> 65
<212> PRT
<213> Artificial Sequence

<220>
<223> modified hirudin

<400> 48

```
Val Val Tyr Thr Asp Cys Thr Glu Ser Gly Gln Asn Leu Cys Leu Cys
 1               5                  10                  15
Glu Gly Ser Val Lys Cys Gly Gln Gly Asn Lys Cys Ile Leu Gly Ser
            20                  25                  30
Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
        35                  40                  45
Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
    50                  55                  60
Gln
65
```

<210> 49
<211> 65
<212> PRT
<213> Artificial Sequence

<220>

<223> modified hirudin

<400> 49
Val Val Tyr Thr Asp Cys Thr Glu Ser Gly Gln Asn Leu Cys Leu Cys
 1   5   10   15
Glu Gly Ser Val Asn Cys Gly Gln Gly Asn Lys Cys Ile Leu Gly Ser
            20   25   30
Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
        35   40   45
Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
    50   55   60
Gln
65

<210> 50
<211> 65
<212> PRT
<213> Artificial Sequence

<220>
<223> modified hirudin

<400> 50
Val Val Tyr Thr Asp Cys Thr Glu Ser Gly Gln Asn Leu Cys Leu Cys
 1   5   10   15
Glu Gly Ser Val Pro Cys Gly Gln Gly Asn Lys Cys Ile Leu Gly Ser
            20   25   30
Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
        35   40   45
Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
    50   55   60
Gln
65

<210> 51
<211> 65
<212> PRT
<213> Artificial Sequence

<220>
<223> modified hirudin

<400> 51
Val Val Tyr Thr Asp Cys Thr Glu Ser Gly Gln Asn Leu Cys Leu Cys
 1   5   10   15
Glu Gly Ser Val Gln Cys Gly Gln Gly Asn Lys Cys Ile Leu Gly Ser
            20   25   30
Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
        35   40   45
Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
    50   55   60
Gln
65

<210> 52

<211> 65
<212> PRT
<213> Artificial Sequence

<220>
<223> modified hirudin

<400> 52
Val Val Tyr Thr Asp Cys Thr Glu Ser Gly Gln Asn Leu Cys Leu Cys
 1   5   10   15
Glu Gly Ser Val Arg Cys Gly Gln Gly Asn Lys Cys Ile Leu Gly Ser
            20   25   30
Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
        35   40   45
Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
    50   55   60
Gln
65

<210> 53
<211> 65
<212> PRT
<213> Artificial Sequence

<220>
<223> modified hirudin

<400> 53
Val Val Tyr Thr Asp Cys Thr Glu Ser Gly Gln Asn Leu Cys Leu Cys
 1   5   10   15
Glu Gly Ser Val Val Cys Gly Gln Gly Asn Lys Cys Ala Leu Gly Ser
            20   25   30
Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
        35   40   45
Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
    50   55   60
Gln
65

<210> 54
<211> 65
<212> PRT
<213> Artificial Sequence

<220>
<223> modified hirudin

<400> 54
Val Val Tyr Thr Asp Cys Thr Glu Ser Gly Gln Asn Leu Cys Leu Cys
 1   5   10   15
Glu Gly Ser Val Val Cys Gly Gln Gly Asn Lys Cys Asp Leu Gly Ser
            20   25   30
Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
        35   40   45
Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
    50   55   60

Gln
65

<210> 55
<211> 65
<212> PRT
<213> Artificial Sequence

<220>
<223> modified hirudin

<400> 55
Val Val Tyr Thr Asp Cys Thr Glu Ser Gly Gln Asn Leu Cys Leu Cys
 1   5   10   15
Glu Gly Ser Val Val Cys Gly Gln Gly Asn Lys Cys Glu Leu Gly Ser
            20   25   30
Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
        35   40   45
Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
    50   55   60
Gln
65

<210> 56
<211> 65
<212> PRT
<213> Artificial Sequence

<220>
<223> modified hirudin

<400> 56
Val Val Tyr Thr Asp Cys Thr Glu Ser Gly Gln Asn Leu Cys Leu Cys
 1   5   10   15
Glu Gly Ser Val Val Cys Gly Gln Gly Asn Lys Cys Gly Leu Gly Ser
            20   25   30
Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
        35   40   45
Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
    50   55   60
Gln
65

<210> 57
<211> 65
<212> PRT
<213> Artificial Sequence

<220>
<223> modified hirudin

<400> 57
Val Val Tyr Thr Asp Cys Thr Glu Ser Gly Gln Asn Leu Cys Leu Cys
 1   5   10   15
Glu Gly Ser Val Val Cys Gly Gln Gly Asn Lys Cys His Leu Gly Ser

```
            20                  25                  30
Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
        35                  40                  45
Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
    50                  55                  60
Gln
65


<210> 58
<211> 65
<212> PRT
<213> Artificial Sequence

<220>
<223> modified hirudin

<400> 58
Val Val Tyr Thr Asp Cys Thr Glu Ser Gly Gln Asn Leu Cys Leu Cys
 1               5                  10                  15
Glu Gly Ser Val Val Cys Gly Gln Gly Asn Lys Cys Lys Leu Gly Ser
            20                  25                  30
Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
        35                  40                  45
Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
    50                  55                  60
Gln
65


<210> 59
<211> 65
<212> PRT
<213> Artificial Sequence

<220>
<223> modified hirudin

<400> 59
Val Val Tyr Thr Asp Cys Thr Glu Ser Gly Gln Asn Leu Cys Leu Cys
 1               5                  10                  15
Glu Gly Ser Val Val Cys Gly Gln Gly Asn Lys Cys Asn Leu Gly Ser
            20                  25                  30
Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
        35                  40                  45
Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
    50                  55                  60
Gln
65


<210> 60
<211> 65
<212> PRT
<213> Artificial Sequence

<220>
<223> modified hirudin
```

<400> 60
Val Val Tyr Thr Asp Cys Thr Glu Ser Gly Gln Asn Leu Cys Leu Cys
 1   5   10   15
Glu Gly Ser Val Val Cys Gly Gln Gly Asn Lys Cys Gln Leu Gly Ser
            20   25   30
Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
        35   40   45
Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
    50   55   60
Gln
65

<210> 61
<211> 65
<212> PRT
<213> Artificial Sequence

<220>
<223> modified hirudin

<400> 61
Val Val Tyr Thr Asp Cys Thr Glu Ser Gly Gln Asn Leu Cys Leu Cys
 1   5   10   15
Glu Gly Ser Val Val Cys Gly Gln Gly Asn Lys Cys Arg Leu Gly Ser
            20   25   30
Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
        35   40   45
Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
    50   55   60
Gln
65

<210> 62
<211> 65
<212> PRT
<213> Artificial Sequence

<220>
<223> modified hirudin

<400> 62
Val Val Tyr Thr Asp Cys Thr Glu Ser Gly Gln Asn Leu Cys Leu Cys
 1   5   10   15
Glu Gly Ser Val Val Cys Gly Gln Gly Asn Lys Cys Ser Leu Gly Ser
            20   25   30
Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
        35   40   45
Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
    50   55   60
Gln
65

<210> 63
<211> 65
<212> PRT

<213> Artificial Sequence

<220>
<223> modified hirudin

<400> 63
Val Val Tyr Thr Asp Cys Thr Glu Ser Gly Gln Asn Leu Cys Leu Cys
 1   5   10   15
Glu Gly Ser Val Val Cys Gly Gln Gly Asn Lys Cys Thr Leu Gly Ser
            20   25   30
Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
        35   40   45
Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
    50   55   60
Gln
65

<210> 64
<211> 65
<212> PRT
<213> Artificial Sequence

<220>
<223> modified hirudin

<400> 64
Val Val Tyr Thr Asp Cys Thr Glu Ser Gly Gln Asn Leu Cys Leu Cys
 1   5   10   15
Glu Gly Ser Val Val Cys Gly Gln Gly Asn Lys Cys Ile Ala Gly Ser
            20   25   30
Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
        35   40   45
Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
    50   55   60
Gln
65

<210> 65
<211> 65
<212> PRT
<213> Artificial Sequence

<220>
<223> modified hirudin

<400> 65
Val Val Tyr Thr Asp Cys Thr Glu Ser Gly Gln Asn Leu Cys Leu Cys
 1   5   10   15
Glu Gly Ser Val Val Cys Gly Gln Gly Asn Lys Cys Ile Asp Gly Ser
            20   25   30
Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
        35   40   45
Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
    50   55   60
Gln
65

<210> 66
<211> 65
<212> PRT
<213> Artificial Sequence

<220>
<223> modified hirudin

<400> 66
Val Val Tyr Thr Asp Cys Thr Glu Ser Gly Gln Asn Leu Cys Leu Cys
 1   5   10   15
Glu Gly Ser Val Val Cys Gly Gln Gly Asn Lys Cys Ile Glu Gly Ser
            20   25   30
Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
        35   40   45
Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
    50   55   60
Gln
65

<210> 67
<211> 65
<212> PRT
<213> Artificial Sequence

<220>
<223> modified hirudin

<400> 67
Val Val Tyr Thr Asp Cys Thr Glu Ser Gly Gln Asn Leu Cys Leu Cys
 1   5   10   15
Glu Gly Ser Val Val Cys Gly Gln Gly Asn Lys Cys Ile Gly Gly Ser
            20   25   30
Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
        35   40   45
Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
    50   55   60
Gln
65

<210> 68
<211> 65
<212> PRT
<213> Artificial Sequence

<220>
<223> modified hirudin

<400> 68
Val Val Tyr Thr Asp Cys Thr Glu Ser Gly Gln Asn Leu Cys Leu Cys
 1   5   10   15
Glu Gly Ser Val Val Cys Gly Gln Gly Asn Lys Cys Ile His Gly Ser
            20   25   30
Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
        35   40   45

Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
50 55 60
Gln
65

<210> 69
<211> 65
<212> PRT
<213> Artificial Sequence

<220>
<223> modified hirudin

<400> 69
Val Val Tyr Thr Asp Cys Thr Glu Ser Gly Gln Asn Leu Cys Leu Cys
1 5 10 15
Glu Gly Ser Val Val Cys Gly Gln Gly Asn Lys Cys Ile Lys Gly Ser
20 25 30
Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
35 40 45
Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
50 55 60
Gln
65

<210> 70
<211> 65
<212> PRT
<213> Artificial Sequence

<220>
<223> modified hirudin

<400> 70
Val Val Tyr Thr Asp Cys Thr Glu Ser Gly Gln Asn Leu Cys Leu Cys
1 5 10 15
Glu Gly Ser Val Val Cys Gly Gln Gly Asn Lys Cys Ile Asn Gly Ser
20 25 30
Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
35 40 45
Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
50 55 60
Gln
65

<210> 71
<211> 65
<212> PRT
<213> Artificial Sequence

<220>
<223> modified hirudin

<400> 71
Val Val Tyr Thr Asp Cys Thr Glu Ser Gly Gln Asn Leu Cys Leu Cys

```
 1               5                  10                  15
Glu Gly Ser Val Val Cys Gly Gln Gly Asn Lys Cys Ile Pro Gly Ser
            20                  25                  30
Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
        35                  40                  45
Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
    50                  55                  60
Gln
65
```

<210> 72
<211> 65
<212> PRT
<213> Artificial Sequence

<220>
<223> modified hirudin

<400> 72

```
Val Val Tyr Thr Asp Cys Thr Glu Ser Gly Gln Asn Leu Cys Leu Cys
 1               5                  10                  15
Glu Gly Ser Val Val Cys Gly Gln Gly Asn Lys Cys Ile Gln Gly Ser
            20                  25                  30
Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
        35                  40                  45
Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
    50                  55                  60
Gln
65
```

<210> 73
<211> 65
<212> PRT
<213> Artificial Sequence

<220>
<223> modified hirudin

<400> 73

```
Val Val Tyr Thr Asp Cys Thr Glu Ser Gly Gln Asn Leu Cys Leu Cys
 1               5                  10                  15
Glu Gly Ser Val Val Cys Gly Gln Gly Asn Lys Cys Ile Arg Gly Ser
            20                  25                  30
Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
        35                  40                  45
Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
    50                  55                  60
Gln
65
```

<210> 74
<211> 65
<212> PRT
<213> Artificial Sequence

<220>
<223> modified hirudin

<400> 74
Val Val Tyr Thr Asp Cys Thr Glu Ser Gly Gln Asn Leu Cys Leu Cys
 1   5   10   15
Glu Gly Ser Val Val Cys Gly Gln Gly Asn Lys Cys Ile Ser Gly Ser
            20   25   30
Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
        35   40   45
Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
    50   55   60
Gln
65

<210> 75
<211> 65
<212> PRT
<213> Artificial Sequence

<220>
<223> modified hirudin

<400> 75
Val Val Tyr Thr Asp Cys Thr Glu Ser Gly Gln Asn Leu Cys Leu Cys
 1   5   10   15
Glu Gly Ser Val Val Cys Gly Gln Gly Asn Lys Cys Ile Thr Gly Ser
            20   25   30
Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
        35   40   45
Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
    50   55   60
Gln
65

<210> 76
<211> 65
<212> PRT
<213> Artificial Sequence

<220>
<223> modified hirudin

<400> 76
Val Val Tyr Thr Asp Cys Thr Glu Ser Gly Gln Asn Leu Cys Leu Cys
 1   5   10   15
Glu Gly Ser Val Val Cys Gly Gln Gly Asn Lys Cys Ile Leu Gly Ser
            20   25   30
Asp Gly Glu Lys Asn Gln Cys Ala Thr Gly Glu Gly Thr Pro Lys Pro
        35   40   45
Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
    50   55   60
Gln
65

<210> 77
<211> 65
<212> PRT
<213> Artificial Sequence

<220>
<223> modified hirudin

<400> 77
Val Val Tyr Thr Asp Cys Thr Glu Ser Gly Gln Asn Leu Cys Leu Cys
 1   5   10   15
Glu Gly Ser Val Val Cys Gly Gln Gly Asn Lys Cys Ile Leu Gly Ser
            20   25   30
Asp Gly Glu Lys Asn Gln Cys Thr Thr Gly Glu Gly Thr Pro Lys Pro
        35   40   45
Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
    50   55   60
Gln
65

<210> 78
<211> 65
<212> PRT
<213> Artificial Sequence

<220>
<223> modified hirudin

<400> 78
Val Val Tyr Thr Asp Cys Thr Glu Ser Gly Gln Asn Leu Cys Leu Cys
 1   5   10   15
Glu Gly Ser Val Val Cys Gly Gln Gly Asn Lys Cys Ile Leu Gly Ser
            20   25   30
Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Thr Pro
        35   40   45
Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
    50   55   60
Gln
65

<210> 79
<211> 65
<212> PRT
<213> Artificial Sequence

<220>
<223> modified hirudin

<400> 79
Val Val Tyr Thr Asp Cys Thr Glu Ser Gly Gln Asn Leu Cys Leu Cys
 1   5   10   15
Glu Gly Ser Val Val Cys Gly Gln Gly Asn Lys Cys Ile Leu Gly Ser
            20   25   30
Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Ala
        35   40   45
Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu

```
    50                  55                  60
Gln
65


<210> 80
<211> 65
<212> PRT
<213> Artificial Sequence

<220>
<223> modified hirudin

<400> 80
Val Val Tyr Thr Asp Cys Thr Glu Ser Gly Gln Asn Leu Cys Leu Cys
 1               5                  10                  15
Glu Gly Ser Val Val Cys Gly Gln Gly Asn Lys Cys Ile Leu Gly Ser
            20                  25                  30
Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Thr
        35                  40                  45
Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
    50                  55                  60
Gln
65


<210> 81
<211> 65
<212> PRT
<213> Artificial Sequence

<220>
<223> modified hirudin

<400> 81
Val Val Tyr Thr Asp Cys Thr Glu Ser Gly Gln Asn Leu Cys Leu Cys
 1               5                  10                  15
Glu Gly Ser Val Val Cys Gly Gln Gly Asn Lys Cys Ile Leu Gly Ser
            20                  25                  30
Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
        35                  40                  45
Glu Ser His Asn Glu Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
    50                  55                  60
Gln
65


<210> 82
<211> 65
<212> PRT
<213> Artificial Sequence

<220>
<223> modified hirudin

<400> 82
Val Val Tyr Thr Asp Cys Thr Glu Ser Gly Gln Asn Leu Cys Leu Cys
 1               5                  10                  15
```

```
Glu Gly Ser Val Val Cys Gly Gln Gly Asn Lys Cys Ile Leu Gly Ser
            20                  25                  30
Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
        35                  40                  45
Glu Ser His Asn Asn Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
    50                  55                  60
Gln
65
```

<210> 83
<211> 65
<212> PRT
<213> Artificial Sequence

<220>
<223> modified hirudin

<400> 83

```
Val Val Tyr Thr Asp Cys Thr Glu Ser Gly Gln Asn Leu Cys Leu Cys
 1               5                  10                  15
Glu Gly Ser Val Val Cys Gly Gln Gly Asn Lys Cys Ile Leu Gly Ser
            20                  25                  30
Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
        35                  40                  45
Glu Ser His Asn Arg Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Leu
    50                  55                  60
Gln
65
```

<210> 84
<211> 65
<212> PRT
<213> Artificial Sequence

<220>
<223> modified hirudin

<400> 84

```
Val Val Tyr Thr Asp Cys Thr Glu Ser Gly Gln Asn Leu Cys Leu Cys
 1               5                  10                  15
Glu Gly Ser Val Val Cys Gly Gln Gly Asn Lys Cys Ile Leu Gly Ser
            20                  25                  30
Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
        35                  40                  45
Glu Ser His Asn Asp Gly Asp His Glu Glu Ile Pro Glu Glu Tyr Leu
    50                  55                  60
Gln
65
```

<210> 85
<211> 20
<212> PRT
<213> Artificial Sequence

<220>

<223> secretion signal

<400> 85
Met Phe Ser Leu Lys Leu Phe Val Val Phe Leu Ala Val Cys Ile Cys
 1   5   10   15
Val Ser Gln Ala
            20

<210> 86
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<223> secretion signal

<400> 86
Met Val Ser Leu Lys Leu Phe Val Val Phe Leu Ala Val Cys Ile Cys
 1   5   10   15
Val Ser Gln Ala
            20

<210> 87
<211> 15
<212> PRT
<213> hirudo medicinalis

<400> 87
Val Val Tyr Thr Asp Cys Thr Glu Ser Gly Gln Asn Leu Cys Leu
 1   5   10   15

<210> 88
<211> 15
<212> PRT
<213> hirudo medicinalis

<400> 88
Leu Thr Tyr Thr Asp Cys Thr Glu Ser Gly Gln Asn Leu Cys Leu
 1   5   10   15

<210> 89
<211> 15
<212> PRT
<213> hirudo medicinalis

<400> 89
Thr Asp Cys Thr Glu Ser Gly Gln Asn Leu Cys Leu Cys Glu Gly
 1   5   10   15

<210> 90
<211> 15
<212> PRT
<213> hirudo medicinalis

<400> 90
Thr Glu Ser Gly Gln Asn Leu Cys Leu Cys Glu Gly Ser Asn Val
1 5 10 15

<210> 91
<211> 15
<212> PRT
<213> hirudo medicinalis

<400> 91
Gly Gln Asn Leu Cys Leu Cys Glu Gly Ser Asn Val Cys Gly Gln
1 5 10 15

<210> 92
<211> 15
<212> PRT
<213> hirudo medicinalis

<400> 92
Leu Cys Leu Cys Glu Gly Ser Asn Val Cys Gly Gln Gly Asn Lys
1 5 10 15

<210> 93
<211> 15
<212> PRT
<213> hirudo medicinalis

<400> 93
Cys Glu Gly Ser Asn Val Cys Gly Gln Gly Asn Lys Cys Ile Leu
1 5 10 15

<210> 94
<211> 15
<212> PRT
<213> hirudo medicinalis

<400> 94
Ser Asn Val Cys Gly Gln Gly Asn Lys Cys Ile Leu Gly Ser Asp
1 5 10 15

<210> 95
<211> 15
<212> PRT
<213> hirudo medicinalis

<400> 95
Cys Gly Gln Gly Asn Lys Cys Ile Leu Gly Ser Asp Gly Glu Lys
1 5 10 15

<210> 96
<211> 15
<212> PRT

<213> hirudo medicinalis

<400> 96
Gly Asn Lys Cys Ile Leu Gly Ser Asp Gly Glu Lys Asn Gln Cys
 1   5   10   15

<210> 97
<211> 15
<212> PRT
<213> hirudo medicinalis

<400> 97
Cys Ile Leu Gly Ser Asp Gly Glu Lys Asn Gln Cys Val Thr Gly
 1   5   10   15

<210> 98
<211> 15
<212> PRT
<213> hirudo medicinalis

<400> 98
Gly Ser Asp Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr
 1   5   10   15

<210> 99
<211> 15
<212> PRT
<213> hirudo medicinalis

<400> 99
Gly Glu Lys Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro
 1   5   10   15

<210> 100
<211> 15
<212> PRT
<213> hirudo medicinalis

<400> 100
Asn Gln Cys Val Thr Gly Glu Gly Thr Pro Lys Pro Glu Ser His
 1   5   10   15

<210> 101
<211> 15
<212> PRT
<213> hirudo medicinalis

<400> 101
Val Thr Gly Glu Gly Thr Pro Lys Pro Glu Ser His Asn Asp Gly
 1   5   10   15

<210> 102

<211> 15
<212> PRT
<213> hirudo medicinalis

<400> 102
Glu Gly Thr Pro Lys Pro Glu Ser His Asn Asp Gly Asp Phe Glu
1 5 10 15

<210> 103
<211> 15
<212> PRT
<213> hirudo medicinalis

<400> 103
Pro Lys Pro Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro
1 5 10 15

<210> 104
<211> 15
<212> PRT
<213> hirudo medicinalis

<400> 104
Glu Ser His Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr
1 5 10 15

<210> 105
<211> 15
<212> PRT
<213> hirudo medicinalis

<400> 105
Asn Asp Gly Asp Phe Glu Glu Ile Pro Glu Glu Tyr Tyr Leu Gln
1 5 10 15

<210> 106
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> modified hirudin sequence

<400> 106
Cys Ala Ala Gly Ser Asp Gly Glu Lys Asn Gln Cys Val Thr Gly
1 5 10 15

<210> 107
<211> 15
<212> PRT
<213> Artificial Sequence

<220>

<223> modified hirudin sequence

<400> 107
Cys Glu Lys Gly Ser Asp Gly Glu Lys Asn Gln Cys Val Thr Gly
1 5 10 15

<210> 108
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> modified hirudin sequence

<400> 108
Cys Arg His Gly Ser Asp Gly Glu Lys Asn Gln Cys Val Thr Gly
1 5 10 15